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CLINICAL EFFICACY OF SITALIPTIN WITH METMORPHINE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS AND CORONARY HEART DISEASE ON THE BACKGROUND OF STATINS

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Abstract:

Type 2 diabetes mellitus (DM2) is a chronic progressive disease. Experts from the World Diabetes Association predict an increase in the number of patients with diabetes by 2030 by 1.5 times and will reach 552 million people i.e. every 10th inhabitant of the planet will get sick[1]. Half of patients with type 2 diabetes already have complications, including from the cardiovascular system, by the time the disease manifests itself. By the age of 50, almost 50% of diabetic patients have at least one of them unstable angina, myocardial infarction, life-threatening cardiac arrhythmias, and chronic heart failure rapidly develops. In this regard, the main strategy for the treatment of patients with diabetes is to prevent the development of cardiovascular complications, which includes strict control of glycemia, blood pressure, as well as antiplatelet and lipid-lowering therapy.

Despite the fact that strict glycemic control alone does not reduce the risk of myocardial infarction and mortality from it, most epidemiological and pathophysiological studies indicate a worse prognosis and a higher incidence of cardiovascular complications in chronic hyperglycemia. The use of a fixed combination of sitagliptin/metformin plus statins in our study is one of the preferred options for the treatment of type 2 diabetes in patients with a high risk of cardiovascular disease, since type 4 dipeptidyl peptidase inhibitors have a cardioprotective effect.

Keywords:

dipeptidyl peptidase-4 inhibitors, metformin, type 2 diabetes mellitus, coronary heart disease, lipid profile.

Relevance

At present, the increase in the number of patients with diabetes mellitus has acquired the character of an epidemic, resulting in loss of working capacity, early disability and premature death. About 50% of all diabetic patients are in the most active working age of 40–59 years [1,3]. By the age of 50, almost 50% of patients with type 2 diabetes develop at least one of them with unstable angina, myocardial infarction, life-threatening cardiac arrhythmias, and chronic heart failure develops rapidly in 12–22% [2]. Thus, 69% of patients with type 2 diabetes have dyslipidemia, 80% have hypertension, 50–75% have diastolic dysfunction, chronic heart failure (CHF) [1]. Mortality from MI among patients with DM2 is 1.5–2 times higher than among people without this disease [2].

In this regard, the main strategy for the treatment of patients with type 2 diabetes is to prevent the development of cardiovascular complications, which includes strict control of glycemia, blood pressure, as well as antiplatelet and lipid-lowering therapy. The

development of vascular complications of type 2 diabetes is associated with chronic hyperglycemia, so the main goal of complex therapy should be complete compensation of carbohydrate metabolism disorders.

To date, the search for new opportunities for the prevention of compl ications in patients with type 2 diabetes continues, which implies a qualitative and constant control of the level of glycemia without an increase in body weight, the risk of developing hypoglycemia, as well as a negative effect on the heart, kidneys and liver, while maintaining the secretory function of β-cells.

In addition, the attention of the entire diabetic community is also drawn to the cardiovascular safety of hypoglycemic drugs. The data of studies conducted with the use of a combination of metformin + DPP-4 inhibitor is associated with a significantly lower risk of adverse cardiovascular events and mortality [4]. Numerous randomized clinical trials involving sitagliptin / metformin have a strong evidence base that allows you to comprehensively evaluate the hypoglycemic and non-glycemic effects, as well as the safety of use, especially in the group of patients with HF-avEF. (heart failure with an average ejection fraction).

Anti-atherosclerotic properties of DPP-4 inhibitors may be associated with anti-inflammatory activity, improvement of endothelial function, and effects on lipid metabolism. In particular, while taking DPP-4 inhibitors in patients with type 2 diabetes, there was a decrease in the concentration of markers of systemic sluggish inflammation (low grade inflammation), including C-reactive protein, interleukins 1β, 6 and 18, tumor necrosis factor α, secretory phospholipase A2 , macrophage activation marker sCD163[1,4].

The Purpose of the Study:

To determine the clinical efficacy of the use of sitaliptin with metmorphine in a group of patients with type 2 diabetes and coronary artery disease.

Material and Research Methods

The study included 70 patients with a diagnosis of type 2 diabetes and coronary heart disease (CHD) aged 30 to 70 years. Patients of the main group (n-50) were divided into 2 groups depending on the EF (ejection fraction).

The first group - with an average ejection fraction (CHF avEF -40-49%) - n-17.

The second group - with preserved ejection fraction (CHF pEF ≥50%) n- 33.

The control group consisted of patients (n-10) taking glimiperide with different EF (41-50- and higher), which, according to the initial clinical, functional and biochemical characteristics, did not differ from the parameters of the main group.

Work with each patient included: questioning (complaints, anamnesis), physical examination (BMI, as well as examination of the cardiovascular, respiratory, digestive, urinary and endocrine systems).Laboratory and instrumental methods of examination: general analysis of blood and urine, biochemical blood analysis, ECG, echocardiographic

examination of the heart, HM ECG (Holter monitoring of ECG), daily monitoring of adherence by assessing blood pressure, questionnaire of Morski-Grin.

Research Results

In the whole sample, the mean experience of DM2 did not differ between the groups and amounted to 10.05±0.59 and 9.5±0.81 years; according to the number of patients who underwent AMI 7 and 5 ($\chi 2$=0.18); PCI 7 and 7 ($\chi 2$=0); the mean age of patients was 59.3±1.4 and 62.4±2.3 years (P=0.5) in the groups with HF avEF and HF pEF, respectively.

To correct the lipid spectrum, patients were prescribed fixed doses (10-20 mg/day) of rosuvastatin from the moment of admission (many patients (40) were already on a statin). Statin therapy was prescribed for the entire observation period (24 weeks) with compliance control.

Monitoring of the patients' condition (clinical and instrumental data, indicators of lipid and carbohydrate metabolism) was carried out upon admission. Analysis of the studied indicators depending on the achievement of target levels of LDL cholesterol showed the following. The number of patients who reached the target level of LDL-C was higher in the HFavEF group and amounted to (n-9; 53%) versus (n-12; 36%) in the HF pEF group. Although some patients were already initially at the achieved target level, and continued to take statins at the same dose.

According to the analysis of lipid spectrum parameters (table), in patients with HFavEF, the average values of TC were: in the initial state 129±12.17 mg/dl; after a year of observation 110.5±9.92 mg/dl (in relation to the initial state t= 1.177; P=0.09); and in the comparison group with HFpEF: at the beginning of the observation 193.75±9.38 mg/dl; after a year of observation 144.83±1.42 mg/dl (in relation to the initial state t= 5.150; P=0.01). That is, the severity of the decrease in the level of total cholesterol was determined by the level of cholesterol at the beginning of the observation. And the difference in reduction was 18.5±3.69 mg/dL (HFavEF) VS 48.91±7.96 mg/dL (t=-3.46589900; P=0.04).

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Comparing the parameters of LDL cholesterol in the analyzed subgroups, we see the following features. In the group of patients with HFav EF LDL decreased from 54±11.04 mg/dl to 39.75±7.52 mg/dl (t= -1.066; P=0.5) (t= -2.820; P=0 .04), in the HFpEF group from 82.75±15.10 mg/dl (t= -1.183; P=0.5) to 64.16±4.28 mg/dl (t= -1.183; P= 0.5).

Despite a significant difference in the level of reduction between groups (t=2.820; P<0.05). Although this difference was not significant in terms of Δ reduction in LDL-C and amounted to 18.58±10.81 in the group with HF avEF and 14.25±5.02 mg/dL in the group with HF pEF (t=-0.363; P>0, 5).

A similar situation is repeated with the content of triglycerides. Initially, the initial levels of triglycerides differed in subgroups and in the group with HF pEF were significantly higher than in the group with HF avEF 220.83±4.89 mg/dl versus 167.33±19.44 mg/dl (t=-2.667; P=0.04). A distinctive feature is the degree of severity of the level of TG. In the group of patients with the target level of LDL-C with HF pEF, the decrease in TG was pronounced and amounted to 202.66±0.61 mg/dL (t= - 3.679; P<0.05), compared with the decrease in TG in the subgroup with HF pEF 164.55±18.93 mg/dL (t=-0.102; P=0.5). But according to the degree of decrease in the difference in ΔTG in the group with HF avEF, there was no decrease in TG 2.77±11.42 mg/dL (t=-2.667; P=0.04), in comparison with the group of HFpEF 18.16±5, 51 mg/dL (t=-1.213; P=0.4). Perhaps the results obtained can be explained by a decrease in the level of PPG in this subgroup (HF pEF), because they are interconnected.

The eGFR indices in the subgroups did not change for the worse, and amounted before and after treatment in the HFavEF and HFpFR groups, respectively: 66.9±8.32 vs 61.8±5.72 and 69±8.57 vs 74±2 .04.

Biochemical parameters depending on the achievement of target levels of LDL-C (70 mg/dl) in patients with coronary artery disease with DM 2 with H and HFpEF before and after treatment (M±m).

Indicators	HF avEF(n-9)		HF pEF (n-12)	
	Before treatment	After treatment	Before treatment	After treatment
Total cholesterol, mg/dl	141,7±18,7	116±9,58##	193±9,38	144±1,42**
CHLDP, mg/dl	68,4±17,4	43,5±7,64##	82,7±15,1	64,1±4,28
CHHDL,mg/dl	32±2,81	37±3,31	31,9±3,67	35,6±1,02
CHVLDP, mg/dl	32,8±3,54	32±3,75###	77,5±1,02	63±0,61**
TG, mg / dL	167±19,4	164±18,9#	220±4,89	202±0,61**
GFR,ml/min/1.73m ²	66,9±8,32	61,8±5,72	69±8,57	74±2,04
PCI, (number)	7		7	0(χ2)
PICS, (number)	7		5	0,18(χ2)
DM (years)	10,5±0,59		9,5±0,81	
Doses S/M, mg	61,1/705,5± 7,34/82,6	61,1/705,5± 7,34/82,6	62,5/850± 10,2/30,61	54,1/850± 10,2/30,61
Doses statin, mg	18,8±2	19,4±0,55	19,7±4,26	17,9±2,04
Fasting blood glucose, mmol/l	8,6±0,42	7,57±0,42*	11,1±0,75	9±0,97
Postprandial blood glucose, mmol/l	13,6±1,26	10,3±0,52	14,8±2,24	11,6±1,95*
HbA1,%	7,64±0,59	7,28±0,22##	9,8±0,64	8,35±0,31*

*P<0.05; ** P<0.01, *** P<0.001 between baseline and stage of therapy in the analyzed groups.

Conclusion

The increase in blood sugar and lipid index was an interrelated process, and in both groups a positive change in lipid profile was noted as a result of the pleiotropic effect of the drug metformin. In the 1st group 9 (52.9%) and in the 2nd group 12 (36%) patients reached the target level for CHLDLP. CHVLDP and TG in the HF pEF group decreased significantly after treatment compared with the HF aEF group. Blood sugar levels also dropped significantly. Changes in the parameters of the lipid spectrum in patients with HF pEF do not depend on the state of carbohydrate metabolism compensation. While in the group of patients with HF aEF content is 1.3 times lower, especially at the final stage (t=3.061; P=0.003), the CHLDLP in the outcome is 1.6 and after treatment is 2.1 times lower in terms of compared with the group of heart failure with pEF, especially in decompensated patients with the same doses of statins and sitagliptin / metformin.

The combination of sitagliptin/metformin in the regimen of hypoglycemic therapy in patients with type 2 diabetes is well tolerated by patients and did not cause hypoglycemia.

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